



IN REPLYING, ADDRESS THE
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DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
FEDERAL SECURITY AGENCY
PUBLIC HEALTH SERVICE
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(b) (3)

I am enclosing a table which gives data obtained in experiments concerned with the development of tolerance to LSD-25.

Eleven subjects completed these experiments. The first 5 subjects were negroes; the last 6 were white. Two negro subjects, RE and GO, did not complete the experiment because they got into trouble with the authorities (not connected with the LSD experiments). The results obtained with these 2 subjects, for completeness sake, are shown below the totals and the averages. In the control experiment, all the subjects were given water at 9 a.m. and at 9 p.m. On the fourth day, they were given 75 mcg. of LSD-25 at 9 a.m., and questionnaires were filled out hourly for eight hours. Clinical notes on behavior were kept. In the other experiment, patients received increasing doses of LSD-25 (10, 20 and 30 mcg.) at 9 a.m. and 9 p.m. for three days. On the fourth day, they were again tested with 75 mcg. of LSD-25. Half of the patients went through the water routine first; half went through the LSD first.

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Results on the questionnaires were estimated simply by counting the number of positive answers (those scored positive, after being scored negative prior to ingesting the drug). The degree of the symptom so recorded was ignored. "Clinical grades" were assigned by myself on the basis of interviews during the test day and the day following. Criteria for the grades were as follows:

- 0 - Absence of nervousness and apprehension,
- 1 - Nervousness and apprehension without distortion in shape or size of self, other persons, or inanimate objects,
- 2 - Nervousness and apprehension, plus distortions in own body image, other persons, or inanimate objects, but without hallucinations and with retention of insight,
- 3 - Nervousness, apprehension, distortions and elementary hallucinations. True hallucinations may be present, but insight apparently retained,
- 4 - Same as Grade 3, but true hallucinations present and insight lost. Grade 4 is apparently quite rare in my experience.

Tabulated data show that these patients gave an average of 98 positive responses after three days on water and only 22 after three days on LSD-25. In terms of clinical grade, the averages were 1.95 after three days of water, and 0.6 after three days of LSD-25.

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I interpret the data as indicating a very significant degree of tolerance after three days on these small amounts of LSD-25. Tolerance, however, was not complete in 5 of the patients. Two of the patients, FO and GR, had very little response to the 75-mcg. dose, even after three days of water, so the presence or absence of ~~tolerance~~ could not be determined.


I hope to confirm these results, using pupillary, blood pressures and reflex responses, in another experiment which will begin as soon as the dose-effect experiment which is currently underway is completed.

I am currently carrying out another tolerance experiment in which patients will receive one dose of LSD-25 daily during an 8-day period in amounts increasing from 20 to 75 mcg. I believe this particular schedule will result in complete, rather than partial tolerance. If this is true, we will then be in position to attempt to determine how much the dose must be elevated to break through this degree of tolerance.

I am sending a copy of the table and letter to Mr. Kornetsky, whom I am expecting to arrive in Lexington about March 15th.

I have just received your letter of March 5th concerning BOL-148, and three vials have arrived in the mail. This will not permit more than a very preliminary evaluation, but I will give you the results as soon as possible.

Yours very sincerely,


Harris Isbell, M.D.
Director of Research

H:rn
Enclosure

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RESPONSE TO 75 MCG. LSD-25

After 3 days H ₂ O at 0900 and 2100			After 3 days LSD-25 (10, 20, 30 mcg. at 0900 and 2100)	
PATIENT	No. Positive Answers	Clinical Grade	No. Positive Answers	Clinical Grade
FO	18	1/2	7	1/2
BSM	251	3	89	1
GR	5	0	1	0
DO	32	1	15	0
AU	101	2	10	0
FR	120	3	54	2
WA	41	2	30	1
WPR	215	3	16	1
WI	167	3	15	1
DE	97	3	8	0
SIM	34	1	0	0
Total	1,081	21-1/2	245	6-1/2
Average	98	1.95	22	0.6
RE	-	-	0	0
CO	43	2		

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Declassified by 187475
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